THE CORNEAL ENDOTHELIUM AND DESCEMET'S MEMBRANE IN THE IRIDOCORNEAL ENDOTHELIAL SYNDROME*

BY *Jon M. Portis,* MD (BY INVITATION), *Robert L. Stamper,* MD, *William H. Spencer,* MD, AND (BY INVITATION) *Robert G. Webster, Jr,* MD

INTRODUCTION

VARYING DEGREES OF UNILATERAL IRIS STROMAL ATROPHY AND MELANOCYTIC AGgregation accompanied by peripheral anterior synechiae, corneal edema, and elevated intraocular pressure appear to be initiated by degenerative and proliferative changes in the corneal endothelium and manifested clinically as one of three related conditions known individually as essential iris atrophy, as Chandler's syndrome and as the iris nevus (Cogan-Reese) syndrome.[1-12] The endothelial changes are often characterized by central corneal degeneration and accompanied by peripheral proliferation and migration over the trabecular meshwork and anterior surface of the iris. The ultrastructural characteristics of the affected endothelial cells may vary. In several cases they have been observed to have features characteristic of degenerating normal endothelium. However, in others they have also been found to possess epithelial characteristics.[13,14] It is not known whether these morphologic alterations reflect developmental differences from normal endothelium or are forms of adult acquired structural alteration.

Tissue obtained at trabeculectomy, iridectomy, and full thickness keratoplasty from one eye of a patient with shared clinical features of essential iris atrophy and of Chandler's syndrome showed light and electron microscopic evidence of proliferating endothelial cells possessing epithelial

*From the Department of Ophthalmology, Pacific Presbyterian Medical Center, San Francisco, California. Supported in part by Research to Prevent Blindness.

features. Our observations of the posterior portion of Descemet's membrane suggest that this cellular alteration is acquired.

CLINICAL FINDINGS

The patient is a 39-year-old woman with progressive left unilateral glaucoma and iris atrophy, first noted in 1978. No other family members have had glaucoma or corneal abnormalities. When first evaluated in the Department of Ophthalmology at the Pacific Presbyterian Medical Center in 1981, slit lamp examination revealed a diffuse beaten-metal appearance of the left corneal endothelium. Left corneal stromal haze and diffuse epithelial edema were also noted. The left pupil was slightly irregular and there was an area of iris stromal atrophy and pigment epithelial exposure at 10:00 o'clock. A broad area of peripheral anterior synechia formation was visible gonioscopically nasally between 7:00 and 10:00 o'clock. Irregular focal synechiae were seen temporally at 2:00 and at 4:00 o'clock. The intraocular pressures were 15 mm Hg, right eye; 39 mm Hg, left eye, on medical therapy consisting of topical epinephrine and echothiophate as well as systemic acetazolamide. The left optic disc exhibited glaucomatous cupping (cup disc ratio 0.8). The left eye visual field showed generalized contraction and an inferior arcuate scotoma. The right eye showed no abnormalities. An initial clinical diagnosis of left unilateral glaucoma associated with essential iris atrophy and/or Chandler's syndrome was made. Despite medical therapy the left intraocular pressure remained elevated and a trabeculectomy was performed (at 12:00 o'clock) without complication. One week postoperatively, the haziness of the cornea was found to have increased despite intraocular pressure measurements ranging from 3 to 12 mm Hg and it was presumed that endothelial decompensation had been exacerbated by the surgery.

During the subsequent 1½ years, the peripheral anterior synechiae nasally and temporally became broader and the intraocular pressure gradually increased requiring reinstitution of antiglaucoma medication. The left corneal haze persisted and the edematous epithelium developed bullous changed with intermittent rupture of the bullae and pain. Specular microscopy of the left cornea could not be obtained because of stromal and epithelial haze. The right eye showed no specular microscopic abnormalities. On May 17, 1983 a left full thickness keratoplasty, repeat trabeculectomy, and peripheral iridectomy (at 1:00 o'clock) was performed. The trabeculectomy and iris specimens and one-half of the corneal button were processed for light microscopic examination. The remaining half of the corneal button was studied with transmission electron microscopy.

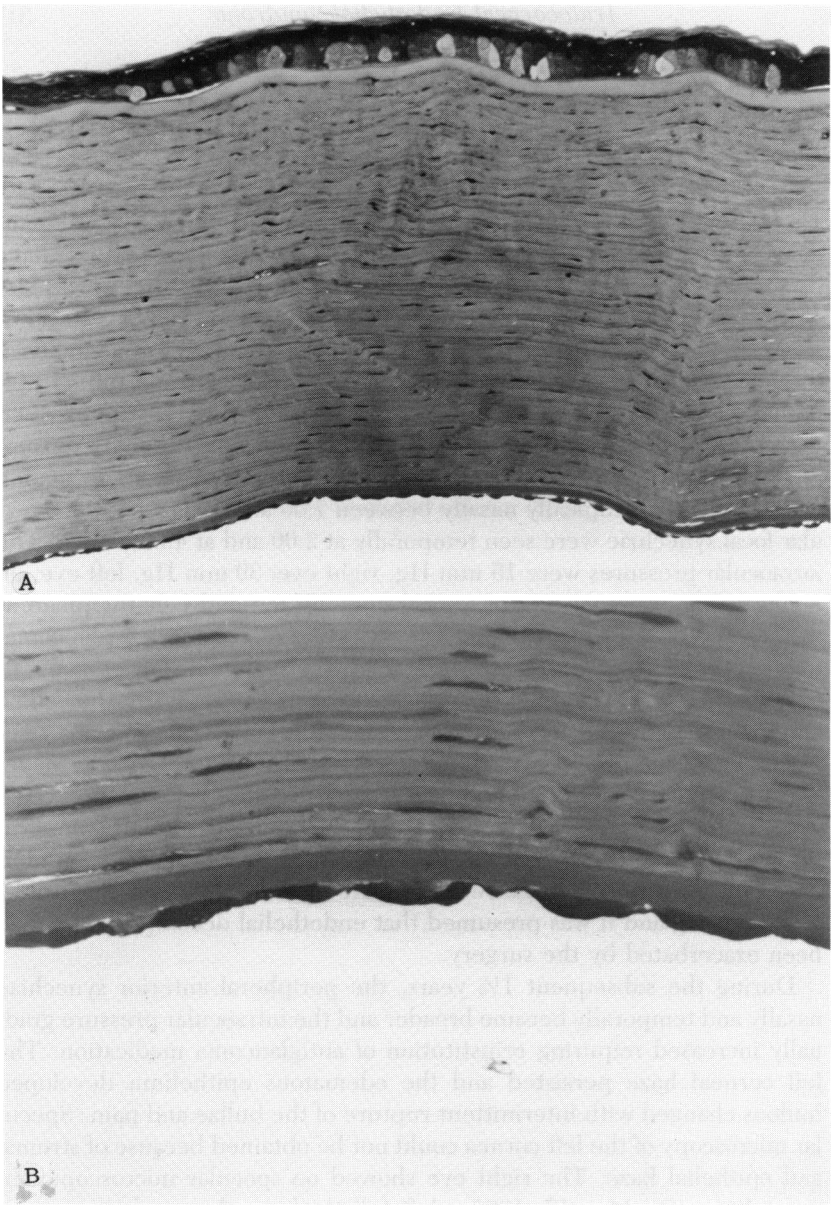


FIGURE 1

A: Section through central portion of cornea. Epithelium and stroma are edematous. Descemet's membrane is of uniform thickness without focal elevations. Endothelial cells are abundant (plastic embedded, 1 μ, toluidine blue, × 25). B: Higher magnification of Fig 1A (plastic embedded, 1 μ, toluidine blue, × 100).

HISTOPATHOLOGIC FINDINGS

LIGHT MICROSCOPY

The corneal epithelium is edematous and several elevated bullae are present. Bowman's layer is intact. The stroma is diffusely thickened and edematous. Descemet's membrane is of uniform thickness without focal elevations (Fig 1A and B). The endothelium is intact and appears to contain a larger number of cells than one would expect to find in age-matched normal endothelium (Fig 1A). The cells do not appear attenuated and no areas of focal absence are observed. In some areas the cells appear double layered (Fig 2).

In the trabeculectomy specimen (Fig 3A) cells morphologically similar to those seen on the cornea cover the inner surface of the trabecular meshwork. Cells of a similar nature are observed on the anterior surface of the fragment of excised iris (Fig 3B).

The trabeculectomy and iridectomy specimens from the procedure performed 1½ years previously show no evidence of abnormal cells over their surface.

ELECTRON MICROSCOPY

Studies are confined to Descemet's membrane and the endothelium. Descemet's membrane exhibits three zones: (1) an anterior zone (adjacent to stroma) approximately 2½ μ thick composed of a lattice of thin collagen filaments with an approximately 110 nm periodic banding pattern. The location, composition, and thickness of this zone is compatible with the component of Descemet's membrane normally produced during perinatal life[15-17]; (2) an intermediate almost homogeneous zone approximately 3.5 to 4.0 μ thick composed of uniform amorphous material characteristic of the component of Descemet's membrane normally produced during youth and adult life (Fig 4A); and (3) an abnormal posterior zone averaging 1.5 μ in thickness composed of material similar to that seen in the intermediate zone but also containing many focal aggregates of fibrillar "wide spacing" collagen (Fig 4A and B). The spacing varies somewhat depending, in part, upon the plane of section and, in part upon the location of the aggregates. The spacing appears closer immediately adjacent to the endothelium (Fig 4B). There is a rather sharp demarcation between zones 2 and 3.

The endothelial cells are increased in number and in several areas they overlap and are arranged in two layers. These cells exhibit overlapping junctions. No unequivocal desmosomal junctions are seen. The cells in the layer adjacent to Descemet's membrane appear partially degenerated

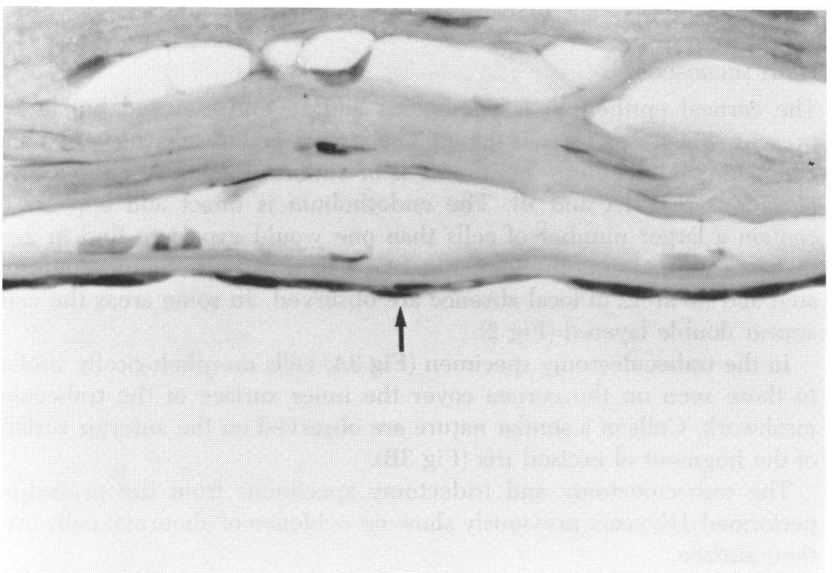


FIGURE 2
Section through central portion of cornea. Some cells (*arrow*) appear double layered (paraffin embedded, 4 μ, H&E, × 40).

and seem to lack a well defined basal layer. The cells in the layer facing the anterior chamber are in a somewhat better state of preservation. They contain surface microvilli, intracytoplasmic tonofilaments and have a larger number of organelles than the deeper layer (Fig 5). No myofibroblast-like features are noted. Both cell layers contain keratin-like filaments. However the cells do not stain with antikeratin antibody.

DISCUSSION

Most of the previously reported histopathologic studies of the cornea from eyes with Chandler's syndrome have shown patchy atrophy and degeneration of the central portions of the endothelium. Rodrigues and co-workers[10] found degenerated endothelial cells with no ultrastructural features suggesting transformation to epithelial-like cells. The histopathologic abnormalities consisted of ruptured or distended cytoplasmic blebs and filopodial processes. Richardson[11] also reported the loss of large numbers of central corneal endothelial cells with exposure of Descemet's membrane. No proliferation of cells was seen and disruption of the endothelial

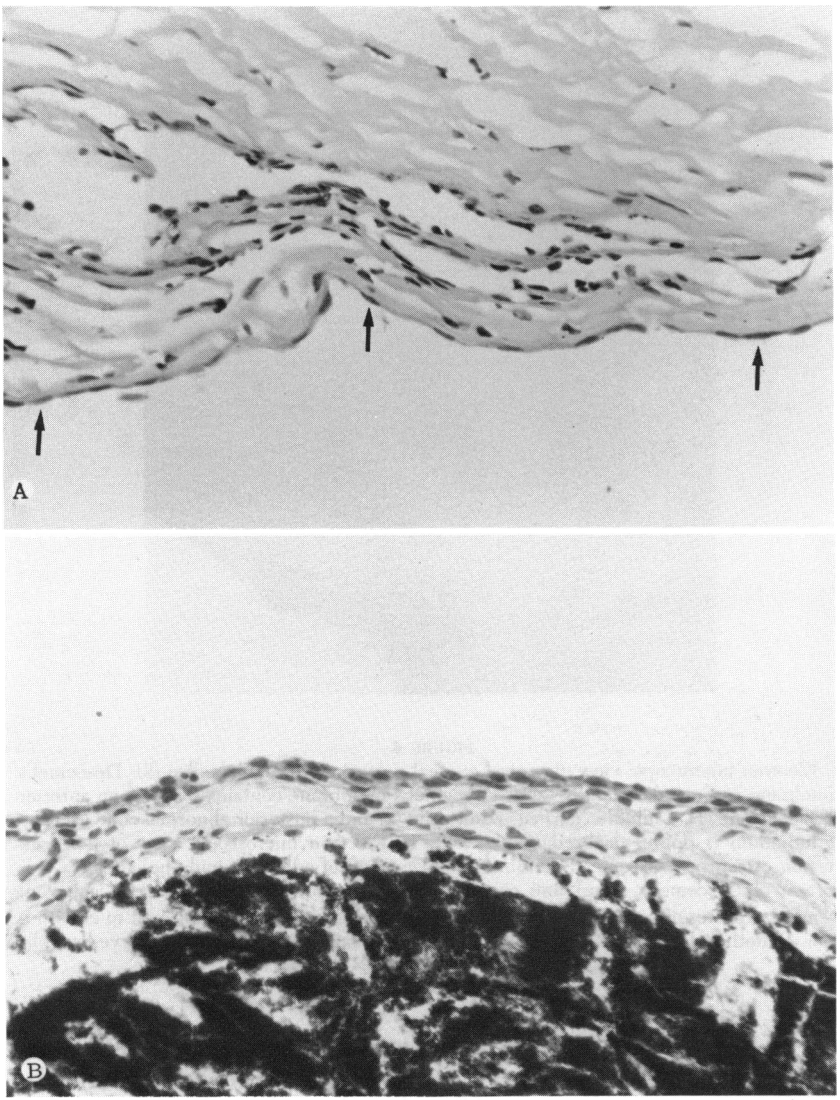


FIGURE 3

A: Section of trabeculectomy specimen. A layer of cells (*arrows*) similar to those on posterior corneal surface covers inner surface of trabecular meshwork (paraffin embedded, 4 μ, H&E, × 40). B: Slightly tangential section of iridectomy specimen. Anterior surface of iris is covered by a layer of cells resembling those seen on endothelial surface of cornea and inner surface of trabecular meshwork. Cells vary from one to four layers. Stroma appears compressed. Pigment epithelial layer has been cut tangentially (paraffin embedded, 4 μ, H&E, × 40).

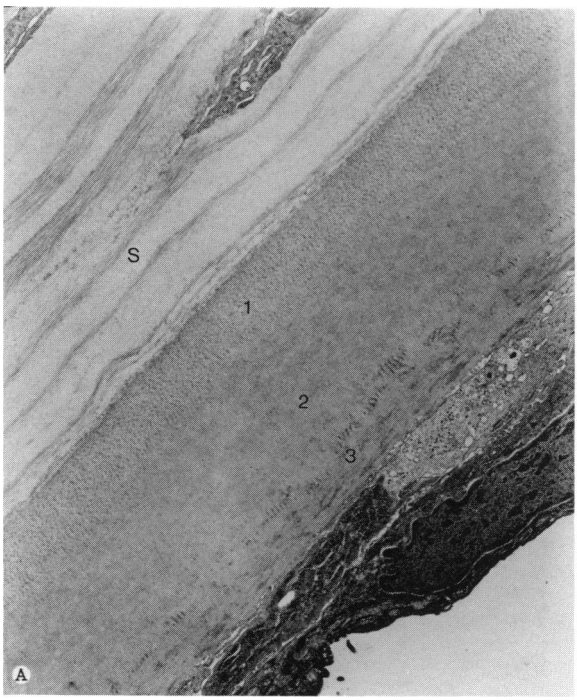
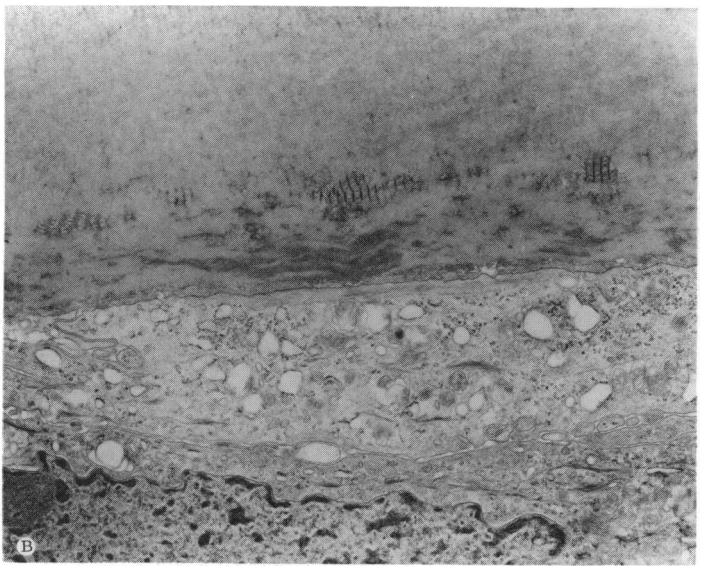


FIGURE 4

A: Electron microscopic view of central corneal posterior stromal lamellae (S). Descemet's membrane and corneal endothelium. Descemet's membrane contains 3 zones, an anterior perinatal zone (1), a middle "normal" adult zone (2) and a posterior abnormal zone (3). The endothelium is double layered (× 10,250). B: Electron microscopic view of posterior portion of central Descemet's membrane and portion of adherent endothelial cells. This portion of Descemet's membrane contains focal aggregates of "wide spacing" collagen. Dense aggregates of banded material with closer spacing are present subjacent to endothelium. Endothelial cells adherent to Descemet's membrane are not as well preserved as cells facing anterior chamber (× 16,500).

barrier was felt to be the cause of corneal edema. In a study of four corneal buttons, Patel and co-workers[12] found the endothelium to be diffusely attenuated, degenerated, and in places focally absent. Quigley and Forster[13] studied a corneal button with endothelial "metaplasia." Multilayering of cells was observed in some areas, while in others there was a single cell layer with occasional gaps. The endothelial cells lacked typical intercellular junctions and exhibited frequent desmosomal connections. The presence of intracytoplasmic filaments and of a large number of microvillous processes on the anterior chamber surface of the



plasma membrane gave the cells an epithelial-like ultrastructural appearance. Hirst and co-workers[14] also noted light microscopic evidence of mild attenuation of the central endothelial cells and ultrastructural as well as immunohistochemical findings characteristic of epithelial cells. Most of the cells were in a single layer but some cells overlapped and others were arranged in two layers.

The light and electron microscopic appearance of the corneal endothelial cells in our case is similar to that reported by Quigley and Forster[13] and by Hirst and co-workers.[14]

Each of these studies show cells with epithelial-like characteristics. In our case the density of central corneal cells is not decreased and Descemet's membrane is covered by relatively large numbers of abnormal cells. The latter seems to be more permeable to aqueous than normal endothelium, since the cornea was edematous despite the abundance of these cells. We considered the possibility that an epithelial ingrowth had occurred during the 1½-year interval between the initial trabeculectomy and the repeat trabeculectomy and keratoplasty. This seems unlikely since the endothelial changes and peripheral anterior synechias were seen clinically before the first trabeculectomy was performed.

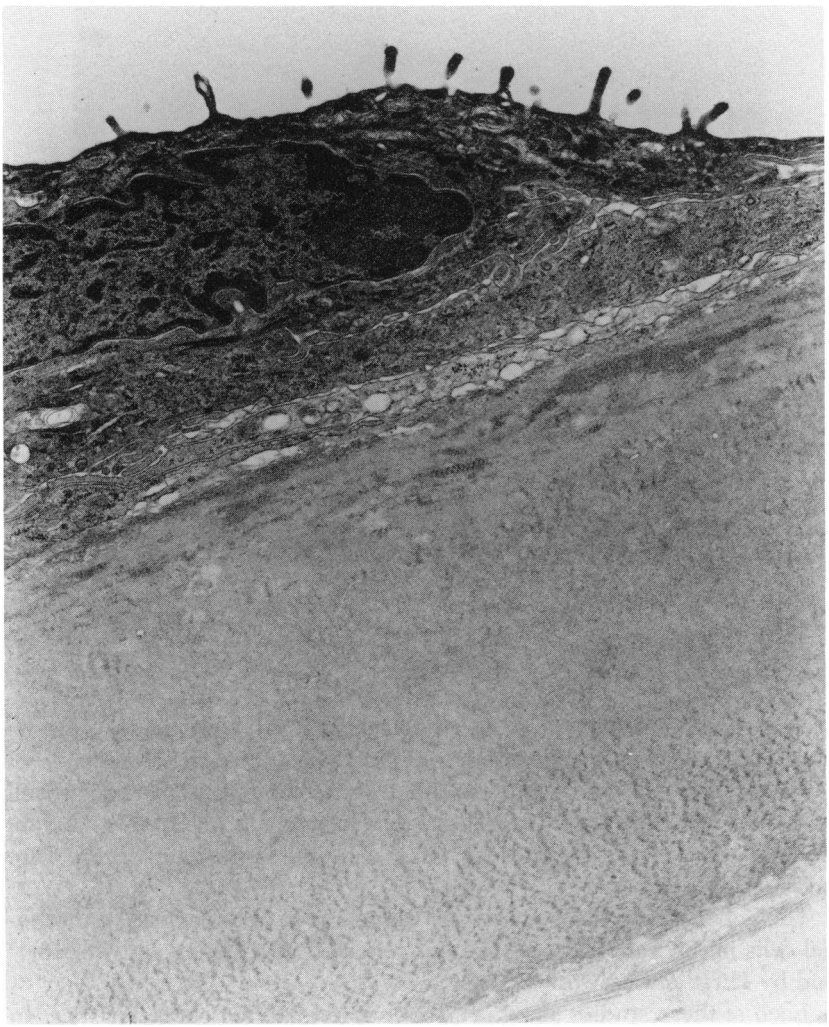


FIGURE 5
Electron microscopic view of central Descemet's membrane and endothelium. Endothelial cell layer facing anterior chamber exhibits surface microvilli (× 12,000).

The sequence of endothelial cellular events in this condition is not known. The clinical manifestations of the process are usually apparent in the cornea before they can be seen to have affected the iris and angle. In our experience, at the time of initial examination of patients who have just been found to have this disease, the corneal endothelium already shows

widespread irregularities when viewed with the slit lamp via specular reflection. The corneal endothelial changes are often more pronounced in one sector, and this usually corresponds with the meridian of focal angle closure and iris traction. Subsequently the process slowly progresses to involve other sectors of the iris and angle structures. These observations suggest that disseminated corneal endothelial degeneration precedes sectoral peripheral endothelial proliferation. Histologic studies are consistent with these observations. When a trabeculectomy is necessary it is usually performed in a sector where the angle appears open. In these areas the pathologic alteration and proliferation of the endothelium may not yet have occurred. It is therefore not surprising that the initial trabeculectomy and iris specimens in our case (performed at 12:00 o'clock) failed to show evidence of abnormal cellular proliferation over their surfaces but these abnormalities were seen in the second trabeculectomy and iris specimen obtained 1½ years later when the process was more advanced. The second procedure was performed at 1:00 o'clock in an area of the angle that appeared to be open but adjacent to an area of synechia formation at 2:00 o'clock. These observations may explain why the trabeculectomy and iris specimens in some of the cases reported by Patel and co-workers[12] failed to show endothelial migration and/or proliferation over their surfaces. In our patient abnormal cells cover the entire central cornea as well as the trabecular meshwork and the iris. No cells are seen that resemble "normal" corneal endothelium and neither of the cell layers covering the posterior surface of the cornea have typical endothelial cell junctions. This suggests either that "normal" corneal endothelium never existed or that the "normal" endothelial cells that were present at birth underwent degeneration and subsequently became partially covered and replaced by cells with acquired epithelial-like features that not only proliferated peripherally but also centrally.

The ultrastructural appearance of Descemet's membrane suggests that the observed endothelial abnormalities are indeed acquired. Normally Descemet's membrane is of uniform thickness and is composed of two zones: a thin anterior striated zone secreted during fetal and perinatal life and a thicker amorphous zone deposited during youth and adult life.[15-17] In abnormal situations, such as Fuchs' endothelial degeneration, an additional nonspecific posterior layer of irregular thickness containing focal inclusions of "wide spacing" collagen and, on occasion, loose fibrillar material has been observed.[18-20] This layer has been assumed to be deposited by "stressed" endothelial cells.[20] Murphy et al[17] noted the similarity of banding periodicity in the prenatal layer and in the "wide spacing" material and they suggest that the latter is deposited by endothe-

lial cells that have reverted to the synthesis of prenatal basement membrane material. In Fuchs' degeneration Descemet's membrane exhibits diffuse as well as focal guttate areas of posterior thickening, probably reflecting localized variation in endothelial cell degeneration and abnormal basement membrane formation. In the iridocorneal endothelial syndrome Descemet's membrane rarely exhibits guttate changes. Possibly the endothelial cell alterations in this condition are less "spotty" than those in Fuchs' degeneration. In our case the presence of normal appearing anterior and middle zones of Descemet's membrane suggests that the endothelium was initially normal. We suspect that the abnormal posterior zone was later deposited by endothelial cells that underwent adult acquired degeneration and partial replacement of proliferating morphologically altered cells that also grew posteriorly over the trabecular meshwork and iris. The factor(s) that initiate these unilateral endothelial cell changes remain a mystery.

SUMMARY

A 39-year-old woman with progressive left unilateral glaucoma associated with corneal edema, iris changes, and peripheral anterior synechia formation underwent a left trabeculectomy and iridectomy in an attempt to control the intraocular pressure. Shortly after surgery the edema worsened despite low intraocular pressure measurements. A repeat trabeculectomy combined with a full thickness keratoplasty was performed 1½ years later. The posterior corneal surface was found to be covered by a partially doubled layer of endothelial cells with ultrastructural features resembling epithelium. Similar cells were not noted on the surface of the initial trabecular meshwork and iris specimens, but were seen on the surface of the specimens obtained at the second trabeculectomy. The anterior and middle portions of Descemet's membrane, formed during perinatal and early adult life, appeared normal, but its posterior portion appeared abnormal. The ultrastructural changes in the endothelial cells and the abnormalities observed in Descemet's membrane suggest that the endothelial cells were initially normal but subsequently acquired epithelial-like features as they degenerated and proliferated. The continued presence of corneal edema despite the hypercellularity of the endothelium suggests that the proliferating cells were permeable to aqueous.

REFERENCES

1. Chandler PA: Atrophy of the stroma of the iris: Endothelial dystrophy, corneal edema, and glaucoma. *Am J Ophthalmol* 1956; 41:607-618.
2. Campbell DG, Shields B, Smith TR: The corneal endothelium and the spectrum of essential iris atrophy. *Am J Ophthalmol* 1978; 86:317-325.
3. Eagle RC, Font RL, Yanoff M, et al: Proliferative endotheliopathy with iris abnormalities: The iridocorneal endothelial syndrome. *Arch Ophthalmol* 1979; 97:2104-2111.
4. Radius RL, Herschler J: Histopathology in the iris-nevus (Cogan-Reese) syndrome. *Am J Ophthalmol* 1980; 89-780-786.
5. Rodrigues MM, Streeten BW, Spaeth GL: Chandler's syndrome as a variant of essential iris atrophy: A clinicopathologic study. *Arch Ophthalmol* 1978; 96:643-652.
6. Scheie HG, Yanoff M: Iris nevus (Cogan-Reese) syndrome: A cause of unilateral glaucoma. *Arch Ophthalmol* 1975; 93:963-970.
7. Scheie HG, Yanoff M, Kellogg WT: Essential iris atrophy: Report of a case. *Arch Ophthalmol* 1976; 94:1315-1320.
8. Shields MB: Progressive essential iris atrophy, Chandler's syndrome and the iris nevus (Cogan-Reese) syndrome: A spectrum of disease. *Surv Ophthalmol* 1979; 24:3-20.
9. Shields MB, Campbell DG, Simmons RJ: The essential iris atrophies. *Am J Ophthalmol* 1978; 85:749-759.
10. Rodrigues MM, Phelps CD, Krachmer JH, et al: Glaucoma due to endothelialization of the anterior chamber angle: A comparison of posterior polymorphous dystrophy of the cornea and Chandler's syndrome. *Arch Ophthalmol* 1980; 98:6188-6196.
11. Richardson TM: Corneal decompensation in Chandler's syndrome: A scanning and transmission electron microscopic study. *Arch Ophthalmol* 1979; 97:2112-2119.
12. Patel A, Kenyon KR, Hirst LW, et al: Clinicopathologic features of Chandler's syndrome. *Surv Ophthalmol* 1983; 27:327-344.
13. Quigley HA, Forster RF: Histopathology of cornea and iris in Chandler's syndrome. *Arch Ophthalmol* 1978; 96:1878-1882.
14. Hirst LW, Green WR, Luckenbach M, et al: Epithelial characteristics of the endothelium in Chandler's syndrome. *Invest Ophthalmol Vis Sci* 1983; 24:603-611.
15. Johnson DH, Bourne WM, Campbell RJ: The ultrastructure of Descemet's membrane. I. Changes with age in normal corneas. *Arch Ophthalmol* 1982; 100:1942-1947.
16. Hogan MJ, Alvarado JA, Weddell JE: *Histology of the Human Eye*. Philadelphia, WB Saunders Co, 1971, pp 93-102.
17. Murphy C, Alvarado J, Juster R: Prenatal and postnatal growth of human Descemet's membrane. *Invest Ophthalmol Vis Sci* 1984; 25:1402-1415.
18. Iwamoto T, DeVoe G: Electron microscopic studies on Fuchs' combined dystrophy: I. Posterior portion of the cornea. *Invest Ophthalmol Vis Sci* 1971; 10:9-28.
19. Hogan MJ, Wood I, Fine M: Fuchs' endothelial dystrophy of the cornea. *Am J Ophthalmol* 1974; 78:363-383.
20. Waring GO: Posterior collagenous layer (PCL) of the cornea. *Arch Ophthalmol* 1982; 100:122-134.

DISCUSSION

Dr W. Richard Green. This study of a case of probable Chandler's syndrome by Portis and co-workers is of interest because it partially confirms the occurrence of epithelial-like characteristics in the corneal endothelium.

In the case that Hirst and co-workers reported we found: endothelial cell polymorphism by specular microscopy and scanning electron microscopy; one or two layers of cells on the posterior surface of the cornea by light and electron

microscopy; aggregates of intracytoplasmic 8 nm filaments, desmosomes and microvillous projections by transmission electron microscopy; and a positive reaction using the monoclonal antikeratin antibody technique developed by Tun Tien Sun (*Proc Natl Acad Sci USA* 1979; 76:2813-2818). In addition, we observed a single layer of cells with similar epithelial characteristics on the anterior surface of the iris.

These features are similar to those demonstrated by the authors, except for the absence of desmosomes and a negative antikeratin reaction in their case. I should like to ask the authors what technique they used to detect keratin, what is the source of the antibody, and were positive and negative controls run at the same time as the patient's tissue?

Richardson first observed epithelial characteristics in the endothelium in Chandler's syndrome. Doctor Hirst and I have studied a current case, and additional cases were alluded to at the recent National Eye Institute Symposium in honor of Doctors Cogan and Kuwabara. In addition to the authors' case, other studies have shown what might be interpreted as incomplete epithelial features—the presence of 8 nm filaments and microvillous projections but the absence of desmosomes.

The case reported by Quigley and Forster is likely posterior polymorphous dystrophy, and not Chandler's syndrome. We have recently studied corneal tissue from a child of their patient and found epithelial features in the posterior cellular layer.

Whether endothelium with epithelial characteristics occur in essential iris atrophy and the iris nevus syndrome is not known. Radius and Herschler have observed compatible intracytoplasmic filaments in one case of the iris nevus syndrome. To date, however, the finding of keratin by the specific monoclonal antikeratin by the specific monoclonal antikeratin antibody technique has not been reported in essential iris atrophy and the iris nevus syndrome.

We go through periods of lumping and splitting in ophthalmology. There are strong and reasonably convincing advocates who lump the three conditions (essential iris atrophy, Chandler's syndrome, and iris nevus syndrome) into the "ICE syndrome" because of the common features of iris atrophy and overgrowth of corneal endothelium. If continued studies verify the presence of epithelial characteristics in the endothelium only in Chandler's syndrome, then there may be reason to begin splitting again.

The lumpers now present evidence that the nevi of the iris nevus syndrome are not nevi, but are rather areas where the anterior surface of the iris is not covered by the ectopic endothelial cell layer. This has been exquisitely demonstrated by Eagle and co-workers (*Br J Ophthalmol* 1980; 64:446-452). In another report, however, Scheie and Yanoff clearly demonstrated diffuse iris nevi in an eye with the iris nevus syndrome. So there are still some unresolved issues concerning this interesting group of diseases that will undoubtedly provoke clinical and histopathology studies for some years to come. I agree with the authors that it is not established whether the changes in the corneal endothelium are congenital or acquired and that we do not know why the endothelium migrates across the angle.

In addition to the three conditions lumped in the ICE syndrome, endothelial overgrowth of the angle with basement-membrane production (descemetization) is seen in a number of unrelated conditions. After post-contusion deformity, rubeosis irides, peripheral anterior synechiae, chronic iritis, and iridocyclitis, Fuchs' heterochromic iridocyclitis, argon laser trabeculoplasty, anterior chamber intraocular lenses, posterior polymorphous dystrophy, and late in aniridia.

I congratulate the authors on an excellent study and I am pleased to have been given the opportunity to render this discussion.

DR M. BRUCE SHIELDS. I was most interested to hear this case study, which represents a group of disorders with which we have been interested for the past decade, and I would like to compliment Doctor Stamper on a very throughtful clinical and histologic study. I was pleased that his findings appear to support what David Campbell and I first described back in the mid 70s regarding the mechanism that binds together these various clinical entities in what is now called the "ICE syndrome." Gordon Klintworth and I first described the ultrastructure of the cornea in this condition at the American Academy meetings several years ago. It was in discussion of that paper that Myron Yanoff first proposed the term, "iridocorneal endothelial syndrome." In those histopathologic cases, we found areas where Descemet's membrane was totally denuded of endothelial cells. This may explain why some eyes retain corneal edema even though the pressure may be quite low following trabeculectomy. Subsequently, in a paper by Doctors Hirst, Quigley, Stark, and myself, we reported a specular microscopy study, in which every single patient had an abnormality of the corneal endothelium, consistent with the thought that this is the fundamental abnormality in the ICE syndrome. While we have not had a large number of the Cogan-Reese cases yet, the Chandler's syndrome and essential iris atrophy group appear to have a specular microscopic appearance, which is a virtually pathognomonic feature of these conditions. We believe that the primary disorder of the corneal endothelium leads to a proliferation of the abnormal tissue seen in the anterior chamber angle and on the iris. It is not surprising that these cells sometimes look different, because we know that the endothelium of the cornea has a propensity for metaplasia and can appear in many different forms. Why patients develop these changes is the big question. Alvarado and associates at the ARVO meeting this year, presented ultrastructural studies, which showed lymphocytes in the endothelial cell layer, and they proposed that this might suggest an infectious etiology. I am told by our pathologists that lymphocytes can appear in association with degenerative endothelial cells, so this may be a nonspecific findings. However, David Campbell suggested to me several years ago that this might be an infectious process, since it always appears in young individuals, it is an acquired condition with no family history, and is unilateral and yet not unilateral. If you look very carefully at the fellow eye by specular microscopy, there is usually a subtle abnormality, and it may be that an infectious process attacks one eye and then interferon or whatever comes along to suppress the full-blown disease in the fellow eye, which may explain the unusual nature of the unilaterality. So we are looking now for the

possibility of some slow virus or other infectious etiology. But I think this information that Doctor Stamper has given us has added a great deal in our continuing search for the final answer to this question, and we thank you very much for that.

DR RICHARD C. TROUTMAN. I enjoyed very much the pathology discussion. However, as a clinician who is often called upon to treat such patients and to assign some prognostic value to the treatment we have noted reduced endothelial cell counts as well as pleomorphism of the endothelium with the specular microscope. I have not observed similar changes in the fellow eye. Possibly, I have not looked as carefully as I might. We have recently tried a treatment which may be of some value clinically, that is, the YAG laser ablation of the peripheral anterior synechiae while we still have sufficiently corneal clarity to perform this procedure. It does seem to reduce for a time the intraocular pressure and to prolong the presurgical course of the disease. It does also prevent the decentration of the pupil which can be a problem when one does penetrating keratoplasty in these patients. I would suggest that you try this. We have been using the Lesag YAG laser with the set of anterior chamber angle mirrored lenses as designed by Fraunfelder.

DR CHARLES PHELPS. Just a quick comment. There has been much confusion in the literature between the group of conditions lumped together under the ICE syndrome and another condition, posterior polymorphous corneal dystrophy. In order to clarify the pathologic differences between the two conditions, we have to be absolutely certain we are providing the pathologist with the correct diagnosis. Thus, I would like to know if you have looked at other members of the family of your patient to rule out posterior polymorphous dystrophy. Posterior polymorphous dystrophy, unlike ICE syndrome, is inherited in an autosomal dominant fashion. Several of our patients with this condition knew of no family history, but when we examined asymptomatic family members, some had classic corneal findings. Posterior polymorphous corneal dystrophy is also bilateral, whereas ICE syndrome is unilateral. However, the fellow eye must be examined with care because the two eyes may differ greatly in severity of involvement.

DR ROBERT STAMPER. I'd like to thank the discussants for their thought-provoking questions. I will take them in reverse order. Doctor Phelps, in answer to your question, we did not get a chance to examine any other members of the family. However, the endothelial changes in the affected eye when the patient was first seen were generalized and no focal changes could be detected by slit lamp. The other eye was and is entirely normal both by slit lamp examination and by specular microscopy. I don't think these findings prove the unilateral nature of her condition nor the absence of posterior polymorphous dystrophy but I do think that they strongly suggest that her clinical condition was not due to posterior polymorphous dystrophy.

Doctor Troutman's observation that applying laser energy to the peripheral anterior synechiae leads to lowered intraocular pressure is very interesting; this approach should be looked into.

In answer to Doctor Shields' question, denudation of Descemet's membrane was not present in any of our sections. And, as mentioned previously regarding Doctor Phelps' comments, my clinical impression was that the endothelium was involved across the entire aspect of the cornea rather than in focal areas. Regarding Doctor Alvarado's work which was most interesting, we saw no lymphocytes in the specimen from our patient. Again, regarding the other eye, we did look at it very carefully both by slit lamp examination and by specular microscopy and could find no abnormality.

Doctor Green, we have no explanation for why there were no desmosomes in our specimen when they were present and beautifully demonstrated in your specimens. The antikeratin antibody was received from the same source as for your study—from Doctors Tang and Rodrigues at the National Institutes of Health. We did run positive and negative controls. The only thing that we did differently was that we did not submit the specimen as a frozen section. This may perhaps explain the difference between our findings and yours. I certainly agree with you that much more work is needed before we can decide whether to lump or split these conditions.

I thank you again for the opportunity of presenting and discussing this paper.